

Amendments to the Specification:

Please replace the paragraph beginning at page 5, line 11 with the following amended paragraph: Figure 2(a) 2(A) and Figure 2(b) 2(B) illustrate the effects of pretreatment with ADNF polypeptides on fetal growth restriction and microcephaly. Fetal weights ~~2(a)~~ 2(A) and fetal brain weights ~~2(b)~~ 2(B) for each pregnant female were obtained at E18. Pretreatment with NAPVSIPQ (SEQ ID NO:2) + SALLRSIPA (SEQ ID NO:1) prevented the growth restriction associated with alcohol treatment. Comparisons are made to the alcohol group, overall ANOVA is $p < 0.001$. Post-hoc Fishers tests were performed, with the * groups significantly different than the alcohol group. Sample size was the number of litters. The mean from each litter was used for statistical analysis and represents on average 8-10 fetuses. The sample sizes were control (32), alcohol (27), NAPVSIPQ (SEQ ID NO:2) + alcohol (24), NAPVSIPQ (SEQ ID NO:2) + NAPVSIPQ (SEQ ID NO:2) + alcohol (17), SALLRSIPA (SEQ ID NO:1) + alcohol (11), VIP+alcohol (17), NAPVSIPQ (SEQ ID NO:2) + SALLRSIPA (SEQ ID NO:1) + alcohol (19), and NAPVSIPQ (SEQ ID NO:2) + SALLRSIPA (SEQ ID NO:1) alone (19).

Please replace the paragraph beginning at page 6, line 3 with the following amended paragraph: The phrase "ADNF polypeptide" refers to one or more activity dependent neurotrophic factors (ADNF) that have an active site comprising the amino acid sequence of SALLRSIPA (SEQ ID NO:1) or NAPVSIPQ (SEQ ID NO:2), or conservatively modified variants thereof that have neurotrophic/neuroprotective activity as measured with *in vitro* cortical neuron culture assays described by, *e.g.*, Hill *et al.*, *Brain Res.* 603, 222-233 (1993); Venner & Gupta, *Nucleic Acid Res.* 18, 5309 (1990); and Peralta *et al.*, *Nucleic Acid Res.* 18, 7162 (1990); Brenneman *et al.*, *Nature* 335, 636 (1988); or Brenneman *et al.*, *Dev. Brain Res.* 51:63 (1990); Forsythe & Westbrook, *J. Physiol. Lond.* 396:515 (1988). An ADNF polypeptide can be an ADNF I polypeptide, an ADNF III polypeptide, their alleles, polymorphic variants, or interspecies homolog, or any subsequences thereof that exhibit neuroprotective/neurotrophic action on, *e.g.*, neurons originating in the central nervous system either *in vitro* or *in vivo*.

Please replace the paragraph beginning at page 13, line 13 with the following amended paragraph:

Another example of algorithm that is suitable for determining percent sequence identity and sequence similarity is the BLAST algorithm, which is described in Altschul *et al.*, *J. Mol. Biol.* 215:403-410 (1990). Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (<http://www.ncbi.nlm.nih.gov/>) (www.ncbi.nlm.nih.gov/). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul *et al.*, *supra*). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W, T, and X determine the sensitivity and speed of the alignment. The BLAST program uses as defaults a word length (W) of 11, the BLOSUM62 scoring matrix (*see* Henikoff & Henikoff, *Proc. Natl. Acad. Sci. USA* 89:10915 (1989)) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a comparison of both strands.

Please replace the paragraph beginning at page 26, line 4 with the following amended paragraph: Methods of non-viral delivery of nucleic acids include lipofection, microinjection, biolistics, virosomes, liposomes, immunoliposomes, polycation or lipid:nucleic acid conjugates, naked DNA, artificial virions, *and* agent-enhanced uptake of DNA. Lipofection is described in, *e.g.*, U.S. Patent No. 5,049,386, U.S. Patent No. 4,946,787; and U.S. Patent No. 4,897,355) and lipofection reagents are sold commercially (*e.g.*, ~~TransfectamTM and LipofectinTM~~) (*e.g.*, TRANSFECTAMTM (dioctadecylamidoglycyl spermine) and LIPOFECTINTM (cationic liposomes)). Cationic and neutral lipids that are suitable for efficient receptor-recognition

Appl. No. 09/267,511

PATENT

Amdt. dated January 4, 2005

Reply to Office Action of November 4, 2004

lipofection of polynucleotides include those of Felgner, WO 91/17424, WO 91/16024. Delivery can be to cells (*ex vivo* administration) or target tissues (*in vivo* administration).